

PATENT COOPERATION TREATY

PCT

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 22253-67116	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US00/12551	International filing date (day/month/year) 08 May 2000 (08.05.2000)	Priority date (day/month/year) 07 May 1999 (07.05.1999)
International Patent Classification (IPC) or national classification and IPC IPC(7): A61K 31/54, 31/495, 31/50, 39/07; A01N 43/58, 43/60 and US Cl.: 514/223.5, 249, 255, 913; 424/246.1		
Applicant THE TRUSTEES OF THE UNIVERSITY OF PENNSYLVANIA		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 4 sheets, including this cover sheet.
- ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 0 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of report with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 07 December 2000 (07.12.2000)	Date of completion of this report 24 August 2001 (24.08.2001)
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703)305-3230	Authorized officer Donna A. Jagoe <i>Donna A. Jagoe</i> Telephone No. (703) 308-0193

Form PCT/IPEA/409 (cover sheet)(July 1998)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/12551

I. Basis of the report

1. With regard to the elements of the international application:*

- ☒ the international application as originally filed.
- ☒ the description:
 - pages 1-38 as originally filed
 - pages NONE, filed with the demand
 - pages NONE, filed with the letter of _____
- ☒ the claims:
 - pages 39-41 as originally filed
 - pages NONE, as amended (together with any statement) under Article 19
 - pages NONE, filed with the demand
 - pages NONE, filed with the letter of _____
- ☒ the drawings:
 - pages 1-20 as originally filed
 - pages NONE, filed with the demand
 - pages NONE, filed with the letter of _____
- ☐ the sequence listing part of the description:
 - pages NONE as originally filed
 - pages NONE, filed with the demand
 - pages NONE, filed with the letter of _____

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item. These elements were available or furnished to this Authority in the following language _____ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in printed form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages NONE
- ☐ the claims, Nos. NONE
- ☐ the drawings, sheets/fig NONE

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/12

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The question whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been and will not be examined in respect of:

- ☐ the entire international application,
☒ claims Nos. 4,8-11,15-18 and 22-35

because:

- ☐ the said international application, or the said claim Nos. _____ relate to the following subject matter which does not require international preliminary examination (*specify*):

- ☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 4,8-11,15-18 and 22-35 are so unclear that no meaningful opinion could be formed (*specify*):

because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

- ☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.
☐ no international search report has been established for said claims Nos. _____

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

- ☐ the written form has not been furnished or does not comply with the standard.
☐ the computer readable form has not been furnished or does not comply with the standard.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/125

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**1. STATEMENT**

Novelty (N)

Claims 1-3, 5-7, 12-14, 19-21, 36,37

YES

Claims NONE

NO

Inventive Step (IS)

Claims 36-37

YES

Claims 1-3, 5-7, 12-14, 19-21

NO

Industrial Applicability (IA)

Claims 1-3, 5-7, 12-14, 19-21, 36-37

YES

Claims NONE

NO

2. CITATIONS AND EXPLANATIONS (Rule 70.7)

Claims 1-3, 5-7, 12-14, 19-21 and 36-37 meet the criteria set out in PCT Article 33(4), because the prior art does not teach or fairly suggest a method for regulating, controlling or modulating aqueous humor secretion comprising the step of administering to ciliary epithelial cells of the aqueous humor comprising administration of a modulator of one or more antiports such as a Na⁺/H⁺ exchanger and a Cl⁻/HCO₃⁻ exchanger.

Claims 1-3, 5-7, 12-14 and 19-21 lack an inventive step under PCT Article 33(3) as being obvious over Burke. The claims are drawn to a method for regulating aqueous humor secretion by administering to ciliary epithelial cells of the aqueous humor, an effective amount of a modulator of one or more antiports such as Na⁺/H⁺ exchanger or Cl⁻/HCO₃⁻. Burke teaches methods and pharmaceutical compositions of Na⁺/H⁺ exchange inhibitors which are useful in lowering intraocular pressure (IOP) and treatment of intraocular hypertension (see abstract). Na⁺/H⁺ exchange inhibitors such as amiloride analogs, improve the ocular hypotensive profile of various alpha 2 agonists when co-administered with the alpha 2 agonist. (column 1, line 56 to column 2, line 5). It differs in that it does not teach the Cl⁻/HCO₃⁻ exchangers of the application.

Claims 1-3, 5-7, 12-14 and 19-21 lack an inventive step under PCT Article 33(3) as being obvious over Stein et al. The claims are drawn to a method for regulating aqueous humor secretion by administering to ciliary epithelial cells of the aqueous humor, an effective amount of a modulator of one or more antiports such as Na⁺/H⁺ exchanger or Cl⁻/HCO₃⁻. Stein et al. teach a method of treating glaucoma comprising administering an effective amount of an oligonucleotide (see abstract). Amiloride, an inhibitor of Na⁺/H⁺ exchange is used to eliminate the possible effects of pH due to the presence of the Na⁺/H⁺ antiporter (column 13, lines 29-31).

Claims 36-37 meet the criteria set out in PCT Article 33(4), because the prior art does not teach or fairly suggest method for regulating aqueous humor secretion by administering to ciliary epithelial cells of the aqueous humor, an effective amount of a modulator of one or more antiports such as Na⁺/H⁺ exchanger or Cl⁻/HCO₃⁻ wherein the anion is transferred into the ciliary epithelial cells of the aqueous humor to block native chloride channels wherein the anion comprises cyclamate.

----- NEW CITATIONS -----

NONE

----- NEW CITATIONS -----